UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,301	12/17/2001	Lisa McKerracher	12552-003001/06447-002-US	1730

26211 7590 03/17/2004

FISH & RICHARDSON P.C.
45 ROCKEFELLER PLAZA, SUITE 2800
NEW YORK, NY 10111

EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,301	MCKERRACHER ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-22* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7-18-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS 7-4-03, 1-21-03, 4-1-02*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group VII in the Paper of 12-9-03 is acknowledged.

2. Claims 1-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the Paper of 12-9-03.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification describes the compound Y-27632 which is disclosed as capable of blocking/inhibiting Rho-associated kinase activity and thereby promoting neurite outgrowth. The claims recite a method of promoting neural growth via delivery of any Y-27632 related compound to the CNS. However, the specification fails to teach either via structure and/or correlating function any other Y-27632 like or related

compounds which exhibit the same effects.

A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself."

Id at 1170, 25 USPQ2d at 1606."

A description of a genus may be achieved by means of a recitation of a representative number of members, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus.

The instant specification discloses, however, a single isolated compound and no other molecule capable of effecting neurite outgrowth. Thus, the specification lacks adequate written description support for the claimed invention.

5. Claim 22 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Y-27632 stimulation of axon outgrowth, does not reasonably provide enablement for any Y-27632 related compound in such method for promoting neural outgrowth. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

The specification exemplifies C. botulinum C3 exoenzyme and Y-27632 stimulation of neurite outgrowth. The specification notes that the specificity of the compounds C3 and Y-27632 are related to inhibition of Rho activity through ADP-

ribosylation of Rho and inhibition of Rho associated kinase. However, the specification fails to teach compounds other than C. botulinum C3 exoenzyme and Y-27632 that are effective to promote neurite outgrowth. Thus, the disclosure is not commensurate in scope with the claims. C3 exoenzyme is structurally unrelated to Y-27632 and the specification is silent as to what other compounds would be expected to provide the activity of promoting neurite out growth as claimed

The specification is required to enable the artisan to practice the invention without further undue experimentation. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the method is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

The instant specification is not enabling because one cannot following the guidance presented therein, practice the claimed method without first making a substantial inventive contribution. The artisan would be required to determine which compounds are suitably related to Y-27632 so as to effect promotion of central nervous axon outgrowth. There is no guidance on this matter within the specification as originally set forth. The artisan must choose the compound and subsequently determine it's suitability for an adequate response. These selections would only after further undue experimentation arrive at the invention now claimed.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 recites promoting neural growth via deliver of y27632 related compounds to a central nervous system. Yet the specification provides no guidance as to those compounds that are Y27632 related or any means for ascertaining them. Thus, the metes and bounds of the compounds encompassed is indefinite to the artisan.

Claim Rejections - 35 USC § 102 or 103

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Sylvain et al., Pediatric Neurology, 10(3):228-32, 1994 as evidenced via Eberlein et al., Br. J. Pharmacol., 133:1172-1180, 2001.

Lovastatin is a recognized rho inhibitor as evidenced via Eberlein et al., Br. J. Pharmacol., 133:1172-1180, 2001. Thus, the compound appears to share the

functional mechanism of neurite outgrowth promoting activity with that of C3 exoenzyme and Y27632. As noted above, there is insufficient structural requirements of a Y27632 related compound to exclude Lovastatin.

Sylvain et al., teach magnetic resonance spectroscopy in Niemann-Pick disease type C: correlation with diagnosis and clinical response to cholestyramine and lovastatin. As disclosed in the abstract, "Niemann-Pick type C is an autosomal-recessive, neurovisceral storage disorder that results from defective cholesterol esterification. Cholesterol-lowering agents have been demonstrated to decrease hepatic lipids in Niemann-Pick type C patients. The objective was to determine the effects of cholesterol-lowering agents on neurologic features and to develop a noninvasive method of monitoring clinical response. A 9-month-old boy with progressive hepatosplenomegaly and neurodevelopmental delay was studied. Water-suppressed proton magnetic resonance spectra from a supraventricular volume of central white and gray matter revealed an abnormal lipid signal. The patient was treated with cholesterol-lowering agents (i.e., cholestyramine, lovastatin). Repeat standardized neurodevelopmental assessments (Peabody and Griffith scales) at 13 and 19 months were normal and magnetic resonance spectra no longer detected the previously observed lipid resonance. Early treatment of Niemann-Pick type C patients with cholesterol-lowering agents appeared to have short-term beneficial effects. Magnetic resonance spectra provided a noninvasive means of monitoring CNS response."

Thus Niemann Pick is a neurodegenerative disease in a patient and the

treatment comprises the administration of a rho inhibitor in the quantity of 0.125 mg/kg daily, gradually increased to 1.0 mg/kg b.i.d. after 8 weeks as set forth in methods, p. 229, column 2, lines 10-16. While the reference teaches systemic administration, such would result in the delivery to the CNS where its effects are noted via the blood circulatory system. While the reference is silent as to whether or not this quantity is sufficient to stimulate neurite outgrowth it is noted that the treatment produced a beneficial response in CNS pathology as assessed via magnetic resonance spectra. Thus, the Sylvain treatment is deemed to be effective to block the degenerative effects of the disease and to promote neurite outgrowth. Therefore the treatment is deemed anticipatory absent convincing factual evidence to the contrary. The Nieman-Pick patient is a patient in need of axon regeneration as a result of the storage disorder. The delivery is via injection thus results in contact with the CNS. Dissemination in the body via the bloodstream would effectively deliver the inhibitor to the axons or their non-neuronal support tissue. Thus, the reference teachings anticipate the claimed invention.

10. Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Varon et al., J. of Neurotrauma 11(5):473-486, 1994 as evidenced by Takahashi et al., Biochem. & Biophys. Res. Communications, 190(3):1156-62, 1993.

Varon et al., teach two models a septo-hippocampal lesion model representing traumatic brain injury and a spinal cord sensory regeneration model representing spinal cord injury. In both models nerve growth factor administration mediates CNS axon regeneration and neurite outgrowth effects in the animal patients. Takahashi et al., teaches that NGF is effective to inhibit the ADP-robosylation of the rho protein via an

indirect mechanism, see in particular abstract and results. The Takahashi reference evidences that NGF exhibits rho inhibiton and thus shares the same mechanism as C3 exoenzyme and Y27632. As claimed, a Y27632 related compound is unlimited structurally and therefore the NGF molecule may qualify as a Y27632 related compound. Thus, the reference teachings anticipate the claimed invention

Status of Claims

11. No claims are allowed.

Conclusion

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (571) 272-0887.

Sharon L. Turner, Ph.D.
2-24-04